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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,869	12/05/2003	Fred H. Mermelstein	02521/100K106-US1	8490

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 01/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,869	MERMELSTEIN ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *25-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/08/04,03/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-24 and 40-41, drawn to a pharmaceutical composition comprising NMDA antagonist and preservative in a suitable carrier.

II. Claims 25-39, drawn to a process of using said composition.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process for using the product as claimed can be practiced with another materially different product (e.g., opioids, bombesin analogs, capsaicinoids, muscamic agonist and antagonist, NSAIDS, steroids, etc...).

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

2. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.

Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01

3. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species of preservative from (i) "organic acids or esters" (ii) "alcohols, polyols and phenols", (iii) "alkyl paraben", (iv) "cresol" or (v) "benzalkonium chloride, chlorhexidine, imdurea, alpha tocopherol

and EDTA" under the instant claims of the elected Group. Moreover, whatever specific compound is ultimately elected, applicants are required to list all claims readable thereon.

With the election of a specific exemplified compound, a generic concept will be identified by the examiner as the inventive group for examination.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

4. During a telephone conversation with Sandra S. Lee on December 06 a provisional election was made to prosecute the invention of Group I (composition claims) along with benzalkonium chloride as the elected species of preservative. Claims 1 and 10-22 read on the elected species. Confirmation of this election must be made by applicant in replying to this Office action. Claims 2-9 and 23-39 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

7. Acknowledgement is made of applicant's submitting of the information disclosure statements (IDS) on March 24, 2004 and January 08, 2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements (IDS) have been considered by the examiner.

8. With respect to "International Search Report" in the submitted PTO-1449, the information disclosure statement filed March 24, 2004 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 10, 11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger (WO 98/51282).

Unger teaches a pharmaceutical composition comprising a therapeutic such as an anesthetic agent (i.e., ketamine chloride) in combination with a surfactant (i.e.alkyldimethylbenzylammonium chloride (=benzalkonium chloride)) in combination with that is administered to mammals including humans, wherein said composition further comprises

aqueous medium (i.e., water, butter and saline), see page 10, line 1 and claims 1, 6, 7, 9, 29 and 64.

The skilled artisan must "at once envisage" the claimed product from "sufficiently limited or well delineated" number of alternatives (about 14 compounds) covered by the preferred active ingredient "anesthetic" and from the listed suitable surfactants (about 31 agents). When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated.

Although Unger is silent about "the composition does not cause any significant neurotoxicity", such characteristic or property is not limited to interpretation of the composition claim since such property or characteristic is deemed to be inherent to the composition, i.e., it was always there.

10. Claims 1, 10, 17, 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Collier et al. (WO 00/24396).

Collier teaches a composition comprising NMDA receptor antagonist (i.e., eliprodil and ifenprodil) and preservative (i.e., benzalkonium chloride) in a suitable carrier (i.e., water and sodium chloride), wherein benzalkonium is present in said composition in the amount of 0.01% to 5% by weight, preferably 0.01% (page 2, line 20 thru page 3, line 4; Example 3 and 6)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1 and 10-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 1330878 (Bristol Myers Co.) in view of Williams et al. (US 6638981 B2).

GB'878 teaches a composition comprising ketamine and preservative such as benzethonium chloride, wherein the dosage range of ketamine is used from about 1 to 2mg/kg in

intravenous administration or from about 5 to 15mg/kg in intramuscular administration (see especially page 2, lines 29-50).

Williams is being supplied as a reference to demonstrate benzalkoium chloride as functional equivalents to benzethonium chloride (column 15, lines 53-64).

The teaching differs from the claimed invention in (i) use of benzalkonium; (ii) the specific dosage amounts of ketamine, namely "from about 1mg/kg to about 15mg/kg per unit dose" (claim 12), "from about 1.0mg/kg to abut 4.5mg/kg per unit dose delivered I.V. and 6.5mg/kg to about 13mg/kg via intramuscular injection" (claim 13); "from about 0.01 mg/kg to about 1 mg/kg per unit dose" (claim 14); "from about 0.05mg/kg to about 0.7mg/kg per unit dose" (claim 15), "about 10 mg per unit 100 microliter dose" (claim 16); (iii) the specific dosage amounts of benzalkonium, namely "from about 0.001% to about 0.2% per unit dose" (claim 18), "from about 0,07% to about 0.14% per unit dose" (claim 19), "about 0.002%" (claim 20); the specific dosage amounts of ketamine and benzalkonium, "10% ketamine hydrochloride and about 0.002% benzalkonium chloride" (claim 22)

As stated above, GB'878 meets the limitation of claim 1 except that employs benzalkonium quaternary ammonium preservative. However, because these two compounds were art-recognized equivalents at the time of the invention was made in those pharmaceutical arts, one having ordinary skill in the art would have found it obvious to substitute a benzalkonium chloride for benzethonim chloride.

Regarding optimization of known active and inactive ingredients in said composition, those of ordinary skill in the art would have been readily optimized effective dosages of ketamine and/or benzalkonium as determined by good medical practice and the clinical condition

of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulations would have been routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information provided in GB'878 where ketamine is used from about 1 to 2mg/kg in intravenous administration or from about 5 to 15mg/kg in intramuscular administration.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1 and 10-22 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-13 and 24-25 of copending Application No.10/256283. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Both the instantly claimed subject matter and the copending application are drawn to a composition comprising NMDA receptor antagonist and preservative, namely benzalkonium chloride. The scope of the present invention overlaps with the claims in copending application.

Conclusion

13. No Claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614